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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 10/23/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/919,471	WILSON ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39,43-45,50 and 56-61* is/are pending in the application.

4a) Of the above claim(s) *13-15 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,16-18,20-39,43-45,50 and 55-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 14, 2003 has been entered.

The addition of claims 56-61 in the amendments filed July 14, 2003 is acknowledged.

The cancellation of claim 55 in the amendments filed July 14, 2003 is acknowledged.

1-39, 43-45, 50, and 56-61 are pending.

Claims 13-15, and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 3.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for rho kinase inhibitors disclosed in instant specification, page 13, lines 1-9, does not reasonably provide enablement for other rho kinase inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. IN the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define a suitable "rho kinase inhibitor" for use in the instant method. Additionally, Applicant fails to provide information

allowing the skilled artisan to ascertain these compounds without undue experimentation. For example, it is not clear what the degree of rho kinase inhibition that a compound possesses would be useful for the instant method. There is no structural or chemical/physical criteria disclosed. In the instant case, only a limited number of "rho kinase inhibitor" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The physiological function and properties of rho kinase are not even fully understood and thus, the use of any compounds that inhibits rho kinase for treating female sexual dysfunction is unpredictable. Such use would require each embodiment to be individually assessed for physiological activity. The instant claims are so broad that they read on all "rho kinase inhibitor(s)", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for melanocortin peptides disclosed in instant specification, page 13, lines 10-20, does not reasonably provide enablement for other suitable melanocortin peptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. IN the instant case, the specification fails to provide information that would

allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation (See above for the eight factors).

Applicant fails to set forth the criteria that define a suitable "melanocortin peptides" for use in the instant method. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. For example, it is not clear what the degree of affinity to melanocortin receptor that a peptide possesses would be useful for the instant method. There is no structural or chemical/physical criteria disclosed. In the instant case, only a limited number of "melanocortin peptides" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The physiological function and properties of melanocortin receptors and its different receptor subtype are not even fully understood and thus, the use of any compounds that is the analogs of α-MSH for treating female sexual dysfunction is unpredictable. Such use would require each embodiment to be individually assessed for physiological activity. The instant claims are so broad that they read on all " melanocortin peptide(s)", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for endothelin antagonists disclosed in instant specification, page 13, lines 21 – page 14, line 15 does not reasonably provide enablement for other suitable endothelin antagonists. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. IN the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation (See above for the eight factors).

Applicant fails to set forth the criteria that define a suitable "endothelin antagonists" for use in the instant method. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. For example, it is not clear what the degree of antagonistic activities to endothelin receptor that a compound possesses would be useful for the instant method. There is no structural or chemical/physical criteria disclosed. In the instant case, only a limited number of "endothelin antagonists" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The physiological function and properties of different endothelin isoforms are different (e.g., endothelin-A

is mainly for controlling vascular tone and endothelin-B are found in brain that has suspected to have CNS properties). Because of the lack of understanding of different endothelin receptors and the physiology thereof, the use of any compounds that antagonize endothelin in the body for treating female sexual dysfunction is unpredictable. Such use would require each embodiment to be individually assessed for physiological activity. The instant claims are so broad that they read on all "endothelin antagonist(s)", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for selective androgen receptor modulators (SARM) disclosed in instant specification, page 15, lines 7-9 does not reasonably provide enablement for other suitable SARM. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. IN the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation (See above for the eight factors).

Applicant fails to set forth the criteria that define a suitable "SARM" for use in the instant method. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. For example, it is not clear what the degree of selectivity to androgenic receptor that a compound possesses would be useful for the instant method. There is no structural or chemical/physical criteria disclosed. In the instant case, only a limited number of "SARM" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The physiological function and properties of different SARM may be different or tissue-specific, and thus, the use of any compounds that selectively modulate androgenic receptors in the body for treating female sexual dysfunction is unpredictable. Such use would require each embodiment to be individually assessed for physiological activity. The instant claims are so broad that they read on all "SARM(s)", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific exemplified neuropeptides disclosed in instant specification, page 15, lines 10-13, does not reasonably provide enablement for other suitable neuropeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to use the invention commensurate in scope with these claims. IN the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation (See above for the eight factors).

Applicant fails to set forth the criteria that define a suitable "neuropeptides" for use in the instant method. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. For example, it is not clear what neuropeptides would be considered useful for the instant method. There is no structural or chemical/physical criteria disclosed. In the instant case, only a limited number of "neuropeptides" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. It is further noted that the compounds listed in page 15, line 14-16, are not peptides. They are neurotransmitters but they are not peptides. It is not clear what "related opioid peptides" are. The physiological function and properties of different neuropeptides are very different (e.g., for example, different neurokinins having very different distribution and functions in the body, are they considered "neuropeptide" useful in the instant method?) and thus, the use of any compounds that is neuropeptides for treating female sexual dysfunction is unpredictable. Such use would require each embodiment to be individually assessed for physiological activity. The instant claims are so broad that they read on all "

neuropeptide(s)", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the exemplified amino acids disclosed in instant specification, page 15, lines 17-28 does not reasonably provide enablement for other amino acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. IN the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation (See above for the eight factors).

Applicant fails to set forth the criteria that define a suitable "amino acids" for use in the instant method. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. For example, it is not clear what characteristics or properties that an amino acid possesses would be useful for the instant method. There is no structural or chemical/physical criteria disclosed. In the instant case, only a limited number of "amino acids" examples are set forth, thereby failing to provide sufficient working examples. It is not clear what

amino acid derivatives (page 15, line 22) referred to. It is noted that these examples are neither exhaustive, nor define the class of compounds required. Examiner notes that the term "amino acids" referred to compounds that have an amino group and a carboxylic acid group. The physiological function and properties of different amino acids may be different, and thus, the use of any compounds that have an amino acids and a carboxylic acid group in the body for treating female sexual dysfunction is unpredictable. Such use would require each embodiment to be individually assessed for physiological activity. The instant claims are so broad that they read on all " amino acid(s)", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 1-12, 16-18, 20-29, 31-39, 43-45, 50, and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation of "cytokines" in claim 1 is new matter. There is no support found in the instant specification for the use of cytokines in the treatment of female sexual dysfunction.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12, 16-18, 20-39, 43-45, 50, and 55-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams (WO 99/66909) and in view of Place et al. (US Patent 5,877,216), Othmer et al. (US Patent 4,640,921) and Gioco et al. (US Patent 5,565,466) (Adams and Place are references of record in the previous office action).

Adams teaches a method of treating female sexual dysfunction employing a dopaminergic agonist, apomorphine and concomitantly with an androgenic agent such as dihydrotestosteroneand its ester (See claims 1-3, 11-12). Adams also teaches that the androgenic agent may be administered orally (See page 21, line 13-25). Adams also teaches that dihydrotestosterone may be administered prior to or concomitantly with apomorphine (See claims 16-17). Adam also teaches that 480μg/kg dose of one of the androgenic agent, testosterone, 36 hours prior to the administration of apomorphine are effective to alleviate sexual dysfunction or normalize sexual dysfunction in post-menopausal and pre-menopausal women (See page 32, line 10-23).

Adams does not expressly teach the androgenic agent is dihydrotestosterone propionate. Adams does not expressly teach the addition agent to be a prostaglandins or prostaglandin derivative such as carboprost tromethamine. Adams does not expressly teach the addition agent to be administered topically. Adams does not

expressly teach the dosing regimen and dosage of the androgenic agent and the secondary active herein. Adams does not expressly teach the employment of a lipoidal carrier to enhance the bioavailability of the androgenic agent. Adams also teaches that the active agents can be formulated into unit dosage form (See page 22, line 5-11).

Place et al. teaches PGE_0 or carboprost tromethamine topical administration is effective in a method of treating female sexual dysfunction (See claims 5 and 9). Place et al. also teaches steroids such as dihydrotestosterone may be employed with the prostaglandins in the method of treating female sexual dysfunction (See claim 10; also col. 8, line 32-47). Place et al. also teaches an additional agent such as detergent may be incorporated into the female sexual dysfunction treating method in increase the solubility and bioavailability of active agents (See particularly claim 13). Place et al. also teaches that the pharmaceutical composition therein can be formulated into liposomal formulation (See particularly claim 20). Place et al. also teaches that the dosage of prostaglandin for the treatment of female sexual dysfunction would be at least the dosage of dyspareunia treatment which is 50 to 500μg/kg (around 3 to 30mg for an average 60kg female) (see col. 13, line 41-51).

Othmer et al. teaches buspirone is useful in treating both female and male sexual dysfunction (See the abstract).

Gioco et al. teaches the vasodilators such as verapamil (a calcium channel blocker) as useful in modulating human, both male and female, sexual response (See col. 14, line 60 to col. 15, line 19 and claim 9-10; particularly claim 10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ dihydrotestosterone propionate with a second active agent such as PGE_0, carboprost tromethamine, apomorphine, buspirone, or verapamil in the dosage range and regimen herein, in the method of treating female sexual dysfunction. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a lipoidal carrier to enhance the bioavailability of the androgenic agent.

One of ordinary skill in the art would have been motivated to employ dihydrotestosterone propionate with a second active agent such as PGE_0, carboprost tromethamine, apomorphine, buspirone, or verapamil, in the dosage range and regimen herein, in the method of treating female sexual dysfunction because all of the dihydrootestosterone esters are known to be useful in treating female sexual dysfunction. Employing dihydrotestosterone propionate would have been reasonably expected to be similarly useful for treating female sexual dysfunction. Employing a second active agent such as PGE_0, carboprost tromethamine, apomorphine, buspirone, or verapamil into the method of treating female sexual dysfunction would have been reasonably expected to be effective based on the teachings of the cited prior art. Combining two or more agents which are known to be useful to treat female sexual dysfunction individually into a single composition and method useful for the very same purpose is prima facie obvious (See *In re Kerkhoven* 205 USPQ 1069). Furthermore, the optimization of result effect parameters (dosage range, dosing regimens) is obvious as being within the skill of the artisan.

One of ordinary skill in the art would have been motivated to employ a lipoidal carrier to enhance the bioavailability of the androgenic agent because based on Place et al. additive such as detergent can enhance the bioavailability of the active compounds. Therefore, employing a detergent into the liposomal formulation useful for treating female sexual dysfunction would have been reasonably expected to be useful for enhancing the bioavailability of the actives herein.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the activities demonstrated in page 38 and 39 in the instant specification are expected based on the prior art. No convincing and clear unexpected result is seen.

Response to Arguments

Applicant's arguments filed July 14, 2003 averring Adam et al. excludes serotonin agonists have been fully considered but they are not persuasive. Applicant is constructively argues teaching away. Examiner notes that Adam et al. is silent about

serotonin agonists, not excluding them. Therefore, it is not teaching away from the instant invention.

Applicant's arguments filed July 14, 2003 averring the cited prior art's failure to provide motivation to combine various agents in the method of treating female sexual dysfunction have been considered, but are not found persuasive. The motivation to combine the various compounds was provided by the cited prior art, as a whole, since the individual agents are known to be useful for the treatment of female sexual dysfunction, combining them into a single composition or employing them concomitantly for the very same purpose is obvious (See *In re Kerkhoven* 205 USPQ 1069).

Applicant's arguments filed July 14, 2003 with regard to the lack of teaching of Adam and Place in regard to the employment of various active in the instant method of treating female sexual dysfunction have been considered moot in view of the new ground of rejection that additional prior arts are cited in the rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
Patent Examiner
Art Unit 1617